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PERSPECTIVES

The role of penicillin-binding protein 2 (PBP2) in the cephalosporin susceptibility of *Neisseria gonorrhoeae* and the need for consensus in naming of PBP2

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Recently, there has been growing concern about the emergence and transmission of *Neisseria gonorrhoeae* multidrug-resistant clones, especially those displaying reduced susceptibility to cephaloporins, e.g., cefixime and ceftriaxone.[1–3] In addition, increasing reports on treatment failures of oral cefixime, and later of injectable ceftriaxone, currently the recommended first-line antibiotic for gonorrhea treatment in many countries, have raised serious concerns worldwide.[1,4] Genetic mechanisms mediating reduced cephaloporin susceptibility of *N. gonorrhoeae* is complicated, including mutations in several chromosomal genes such as *penA*, the gene that encodes the penicillin-binding protein 2 (PBP2); *porB1*, an outer membrane protein channel related to antibiotic entry; *ponA*, the penicillin-binding protein 1 (PBP1); *pilQ*, the outer membrane secretin PilQ; and *mtrR*, a repressor of the MtrC-MtrD-MtrE efflux pump.

Among them, the polymorphisms in the *penA* allele are the major contributors of resistance to cephaloporins in *N. gonorrhoeae*.[2,4–6] PBP2 is a membrane-bound enzyme involved in cell wall biosynthesis and it is one of the targets of the β-lactam antibiotics. The mutation in different positions of PBP2 may result in various levels of minimal inhibition concentration (MIC) increase. PBP2s with mosaic structure confer significantly higher MIC to cephalosporins than those having non-mosaic structures.[1,2,4–6]

Several reports on the emergence of cephalosporin-resistant gonorrhea have indicated that the resistant strains are mostly clonal and contain specific PBP2 types, such as mosaic types X, XXXIV, and others.[7] Thus, in view of the important role of PBP2 types in cephalosporin resistance, it is essential that the PBP2 types be characterized precisely and named correctly.

We reviewed and summarized the names of PBP2s used in different gonococcal studies during 2005–2011, and found several discrepancies in the naming of PBP2. Since 2005, at least 37 sequence types of PBP2 have been reported.[1,2,4–6,8–12] For PBP2 sequence types I to XXIII (except types X and XII), no conflict in assignment of PBP2 names was found among previous studies. However, for the rest of the PBP2s, disagreements in nomenclature were found: (1) seven PBP2 sequence types have discordant names in different reports; and (2) under the PBP2 type XXIV, there are two alternatives, one is mosaic and the other is nonmosaic (see Table 1). In view of the increasing international transmission of gonococcal strains with reduced susceptibility to cephalosporins, unification in PBP2 nomenclature is needed.

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Table 1 The names of different PBP2 sequence types used in previous studies.

PBP2 name based on ref. 4	Reference	PBP2 name based on refs. 1, 2, 5, and 6	Reference	Other name[a]	Reference
X*[b]	4	XXXV*	5		
XII		XXXVI	5		
XXIV		XXIV	6		
XXV*		XXV*	2	mosaic-3	10
XXVI*		XXVI*	2	mosaic-4	10
XXVII*		XXIV*	2	mosaic-2	10
XXVIII*		XXVII*	2	PBP2 of strain 30/02	8
XXIX*		XXVIII*	1, 2	PBP2 of strain 35/02[c]	8
XXXIII		XXIX	2	PBP2 of strain 188/03	8
XXXV*		XXXVIII*	5		
XXXVI					

[a] The name of a PBP2 sequence type in its source study.
[b] *indicates mosaic PBP2 types.
[c] The PBP2 of strain 35/02 in refs. 1, 2, and 8 was assigned as type XXVIII, but the amino acid sequence of *penA* allele in *N. gonoeehoeae* strain 35/02 (GenBank accession number ZP_06129591) in NCBI was identical to PBP2 type X. We are not sure whether these two alleles are different.

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